REMARKS

Status of the Claims

Claims 1-54 are pending and claims 1-18 and 35-54 are presently under consideration in this application, claims 19-34 having been withdrawn from consideration on the ground that they are allegedly drawn to separate inventions. All the claims presently under consideration stand rejected. After entry of the amendments made herein, claims 1-18 and 35-54 will be pending and claims 1-18 and 35-54 will be under consideration in this application.

35 U.S.C. § 112, first paragraph, rejection

The rejection of claims 1-18 and 35 on the ground of lack of enablement is maintained.

From the comments on page 2, line 15, to page 3, line 5, of the instant Office Action and those in the prior Office Actions, Applicant understands the Examiner's position to be that, while the instant specification (e.g., the experiment described in Example 1) provides support for the MTBN4 polypeptide having *Mycobacterium tuberculosis* specific antigenic properties, it does not do so for the other polypeptides recited by the claims.

Applicant respectfully disagrees with this position and maintains that, in view of the data presented in the specification and the knowledge and skill possessed by those skilled in the art (which is high), such artisans would believe it likely that these additional polypeptides would, like MTBN4, have *Mycobacterium tuberculosis* specific antigenic properties. Indeed, the specificity analysis described in Brusasca et al. (provided as Exhibit A in the Amendment and Response filed December 23, 2003) indicate the correctness of such a belief. Applicant apologizes to the Examiner for not having previously drawn his attention to the specificity study described in the Brusasca et al. article.

Brusasca et al. describes an "experiment of nature" that is in essence the same as the specificity analysis on MTBN4 described in Example 1 of the instant specification. Thus, the article shows that sera from various numbers of subjects infected with *M. tuberculosis* contained antibodies that bound to MTBN1 (RV3871), MTBN2 (Rv3872), MTBN4 (MTSA-10), MTBN7

(Rv3878), and ESAT-6 (a polypeptide that is not recited in the present claims but that, like those that are, is expressed by *M. tuberculosis* but not by BCG). Importantly, in contrast, sera from no control subjects having other mycobacterial infections (e.g., *M. avium* as in the Example 1 experiment) and no "normal" subjects contained such antibodies (page 450, paragraph spanning columns 1 and 2, and Table 1).

Given that none of subjects infected with bacteria relatively closely related to *M. tuberculosis* produced antibodies that bound to the test polypeptides, one skilled in the art would conclude that subjects infected with less closely related bacteria would be even less likely to produce such antibodies. Indeed the tests performed by Brusasca et al. on so-called "normal" subjects support such a conclusion. While such normal subjects may at the time of testing have had no identified infection, all humans are continually exposed to a host of microorganisms, including bacteria of multiple species, and produce antibodies that bind to molecules expressed by such microorganisms.

Given these findings on the MTBN1, 2, 4, and 7 polypeptides, one skilled in the art would consider it unlikely that sera from control subjects (e.g., those exposed to mycobacteria other than *M. tuberculosis*) contain antibodies that bound to the other MTBN polypeptides recited by the claims (i.e., MTBN3, 5, and 8) and that any putative cross-reactivity between the polypeptides recited in the instant claims and polypeptides in any other bacteria would be entirely fortuitous. Such cross-reactivity is a potential problem common to all serological diagnostic tests for microbial infections. The chances of misdiagnosis resulting from such cross-reactivity can be reduced by, for example, testing for other markers of a microbial infection of interest, e.g., symptoms known to be caused by the microbe, x-ray and other imaging analyses, or the presence of antibodies specific for a plurality of molecules produced by the relevant microbe. Nevertheless, in order to expedite prosecution of the instant application, polypeptides MTB3, 5, and 8 (or genes encoding them) have been deleted from the claims.

In light of the above considerations, Applicant respectfully requests that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

35 U.S.C. § 112, second paragraph, rejection

The rejection of claims 36 - 52 is maintained, and claims 53-54 are rejected, on the grounds of indefiniteness. Applicant respectfully traverses the rejection.

Applicant understands the Examiner's position to be that, since claims 36 -52 and 53 - 54 are dependent on rejected claims, they are indefinite. Since, for the reasons given above, the claims on which claims 36-52 and 53 - 54 are dependent are allowable, Applicant submits that the rejection is moot.

CONCLUSIONS

Applicant submits that the pending claims patentably define the invention and request that the Examiner permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's undersigned representative can be reached at the telephone number listed below.

Enclosed is a request for an automatic extension of time, and a check in payment of the extension in time. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 07763-043001.

Respectfully submitted,

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